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OXIDATION OF 4-, 6- AND 7-HYDROXYINDOLES.

Alessandra Napolitano, Marco d'Ischia, Giuseppe Prota*

Department of Organic and Biological Chemistry,
University of Naples
Via Mezzocannone 16, I-80134 Napoli, Italy.

and

Thomas M. Schultz, Leszek J. Wolfram

Lawrence M. Gelb Research Foundation
2, Blachley Road, Stamford, CT, 06902 USA

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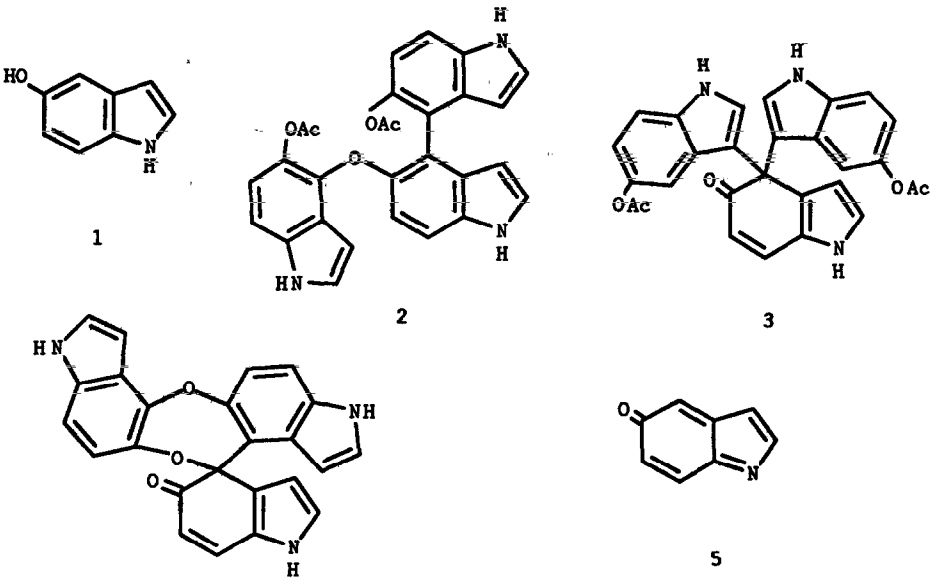
Abstract. Oxidation of 4-, 6- and 7-hydroxyindoles with sodium periodate in phosphate buffer at pH 7.0 leads to complex mixtures of oligomeric products, the majority of which have been isolated and characterised as the O-acetyl derivatives. 7-Hydroxyindole (**6**) gives predominantly the dimers **9** and **10** as well as the trimer **11** and the tetramer **12** in smaller amounts. The 4- and 6-hydroxy isomers **7** and **8** follow less clear-cut reaction paths, characterised by the formation of the oligomers **13-16** and **17-19** respectively, along with polymeric materials. The observed mode of polymerisation of hydroxyindoles **6-8** is apparently consistent with a mechanism involving nucleophilic addition of the starting indoles to the electrophilic positions of transient quinonimine or phenoxonium-like intermediates.

Interest in the oxidation chemistry of hydroxyindoles has been desultory and fragmentary over the years, being mainly centred on the dimerisation reaction of 3-hydroxyindoles (indoxyls), leading to indigo dyes,[1,2] and the polymerisation of 5,6-dihydroxyindoles, which is relevant to the biosynthesis of melanin pigments[3]. Relatively little attention has been devoted to carbocyclic monohydroxyindoles, which occur as integral part of a variety of biologically active compounds, including 5-hydroxytryptamine (serotonin)[4,5], the isomeric 6-hydroxytryptamine[5], the antibiotic gliotoxin[6] as well as a plethora of tryptophan derived alkaloids[7,8,9]. There are reasons to believe that the biological properties of these compounds may be partly related to their susceptibility to undergo oxidation giving rise to highly reactive species[5].A typical example is the postulated activation of the antitumour drugs 9-hydroxyellipticine[10] and (+)-CC-1065[11] through the transient generation of quinonimine and p-quinonimine methide intermediates,

respectively.

Most of what is presently known of the oxidation chemistry of carbocyclic hydroxyindoles derives largely from the studies of Teuber[12] in the 1950's and Remers [13] in the 1960's. These were mainly concerned with the Fremy's salt oxidation of some 4- and 5-hydroxyindole derivatives leading invariably to the formation of 4,5- or 4,7-indolequinones.

In the framework of our continuing studies on the chemistry of hydroxyindoles[14,15], we have recently carried out a detailed investigation of the reactivity of 5-hydroxyindole (1) under biomimetic conditions[16]. In the course of that study , evidence was obtained that on treatment with a variety of oxidising agents 1 undergoes a polymerisation reaction giving rise to a complex mixture of oligomers. These were isolated as the acetyl derivatives and identified as the dimers 5,5'-diacetoxy-4,4'-biindolyl and 5,5'-diacetoxy-3,4'-biindolyl ,the trimer 2, the symmetrical 4,4-bis-(3'-indolyl)-5(4H)-indolone 3 and notably the 1,4-dioxepin-spiro-5(4H)-indolone 4. From consideration of the structure of these compounds, a mechanism for the polymerisation of 1 was proposed involving the intermediacy of the p-quinonimine intermediate 5.



The unexpectedly complex picture of the oxidation chemistry of 5-hydroxyindole which emerged from that study prompted us to extend the

investigation to the other isomeric carbocyclic hydroxyindoles, i.e. 4-, 6-, and 7-hydroxyindole.

Among the various oxidants tested, sodium periodate proved the most suitable in view of its efficiency in effecting complete oxidation of all the substrates under investigation.

Preliminary spectrophotometric analysis showed that the course of the periodate oxidation varies considerably with the substrate used. Thus, in the case of 7-hydroxyindole (**6**), the rapid development of a well defined chromophore at 479 nm was observed, whereas 4-hydroxyindole (**7**) and 6-hydroxyindole (**8**) gave dark pigmented materials, displaying almost featureless UV spectra.

In further experiments, evidence was obtained that the oxidation reaction is first order with respect to the indole substrate and attains its maximum rate at pH values around neutrality. Apparent first order kinetic constants at pH 7.0 were found to be 1.7×10^{-1}, 1.4×10^{-1} and 1.9×10^{-3} s^{-1} for **6**, **7**, and **8**, respectively, indicating that the first two indoles are much more prone to oxidation than the latter.

With this background available, a preparative scale oxidation was initially attempted on **6** in a buffered solution at pH 7.0 using one molar equivalent of periodate. Direct analysis of the chromophoric species formed proved to be difficult owing to their marked instability under the usual chromatographic conditions, and we eventually resolved to adopt an isolation procedure already introduced in related investigations[14,17]. This involves reduction of the oxidation mixture with sodium dithionite, followed by acetylation of the ethyl acetate extractable fraction.

7-Hydroxyindole (6).

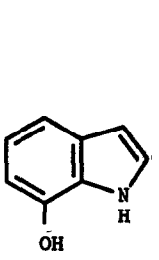
Analysis of the acetylated mixture revealed the presence of a relatively simple pattern of products, the major of which were isolated after repeated chromatographic fractionation.

Two of these were readily identified as the dimers **9** and **10** on the basis of spectral analysis.

A third more polar compound proved to be a trimer made up of two terminal indole units linked through the 4- and 3-position to the 4- and 6- positions of a central indole ring (^1H and ^{13}C NMR evidence). Of the two possible structures which could fit these data , structure **11** was chosen on the basis of the significant NOED effect observed between the H-3′ proton resonance and the doublet arising from the H-2 proton.

The major component of the mixture (M^+ at m/z 694) was formulated as the symmetrical tetramer **12** . The ^1H NMR spectrum exhibited, in addition

to two acetyl groups, seven resonances in the aromatic region, four of which attributable to a C-3 substituted indole unit, and the remaining three to a C-4,C-6 disubstituted indole ring. The exact mode of linking of the indole units followed from NOED experiments, indicating a spatial proximity of the H-3'(H-3") and the H-2 (H-2''') protons .



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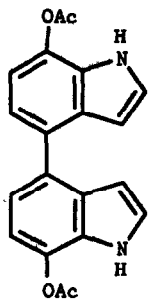

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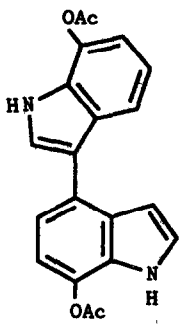

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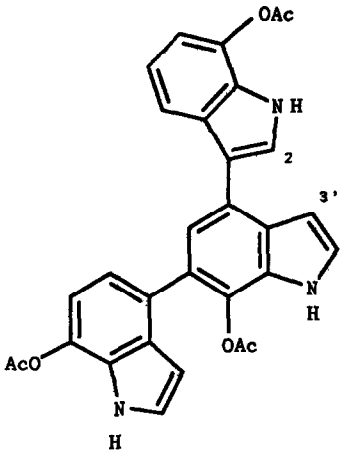

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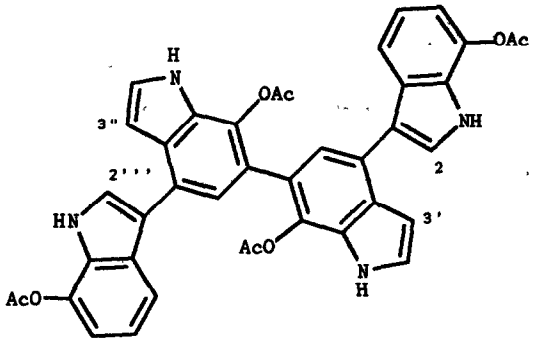

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4-Hydroxyindole (7).

Reduction and acetylation of the oxidation mixture from 7 revealed a highly complex pattern of products, four components of which could be isolated after fractionation by flash chromatography and preparative TLC.

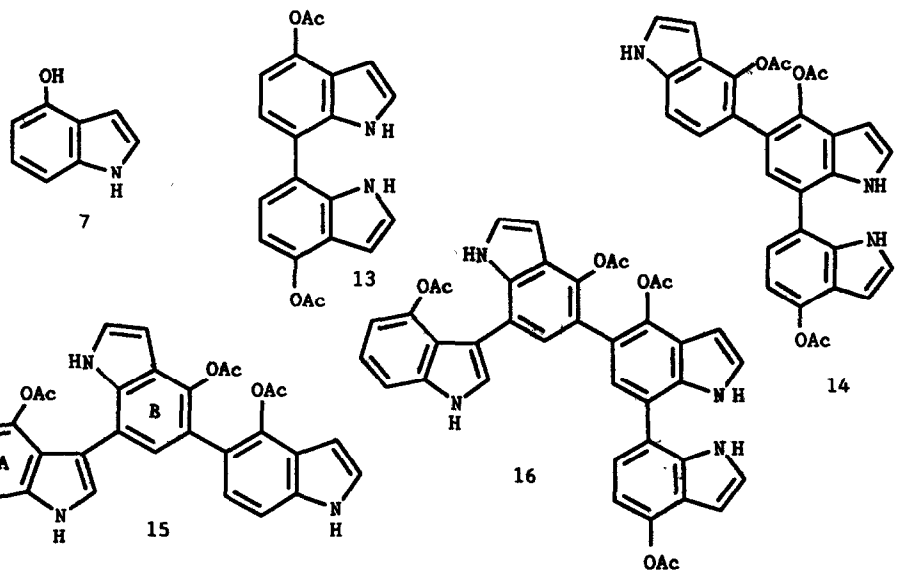
The less polar compound was formulated as the symmetrical dimer 13 by straightforward analysis of the ^{1}H and ^{13}C NMR spectra.

Two other components of the mixture exhibited virtually similar mass spectra with molecular ion peaks at m/z 521, suggesting trimeric structures. In the less abundant isomer, the indole units were apparently linked through the 5- and 7- positions, as shown by the ^{1}H NMR spectrum. The considerable overlap of the signals arising from the N-H, H-2, H-3 protons of the two C-7 substituted indole rings pointed to the highly

symmetrical structure **14** rather than the alternative 4,4',4"-triacetoxy-5,7':5',7"-terindolyl.

Spectral data of the other trimer were consistent with two isomeric structures in which a central indole unit was linked through the 5- and 7- positions to the 3- and 5- positions of the outer indole rings. Attempts to discriminate between the two isomers by spectral techniques, including NOED and 2D-heterocorrelation long-range experiments were unsuccessful. Nevertheless, on the basis of a comparison of the NMR spectral features with those of the dimer **13** and the trimer **14** , the compound was tentatively formulated as **15**. In accordance with the proposed structure is the unusual upfield resonance of the acetyl group of the indole unit A (δ 1.32) which would be expected to fall within the shielding cone of indole unit B.

The fourth oligomer, which could be obtained only in very minute amounts, proved to be a tetramer (M^+ at m/z 694). The ^1H NMR spectrum revealed the presence of the characteristic pattern of resonances of the trimer **14**, with the exception of the H-7 proton, plus four additional signals due to a C-3 substituted indole ring. These data could only be accommodated by structure **16** which notably comprises the structures of both trimers **14** and **15**. In line with this formulation is the observed shielding of one of the acetyl groups (δ 1.31) which apparently results from the same structural arrangement present in trimer **15**.

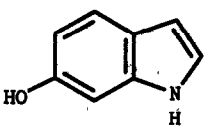


6-Hydroxyindole (8).

Periodate oxidation of **8** under the usual conditions led to a brownish-black polymeric material which could not be analysed even after reduction and acetylation. A more definite pattern of products could be obtained using half a molar equivalent of periodate, under which conditions only partial consumption of the starting material takes place.

From the less polar fractions of the mixture two dimers of **8** were isolated, the most abundant of which was assigned structure **17** and the other structure **18**.

Another major component of the mixture was identified as the trimer **19** on the basis of its ^{1}H NMR spectrum exhibiting, besides the resonances of two C-7 substituted indole units, an H-3 double doublet (δ 6.84), an H-7 doublet (δ 7.42) and an H-4 singlet (δ 7.59) for a 2,5-disubstituted central indole ring.



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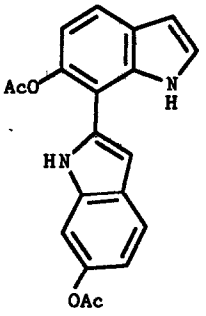

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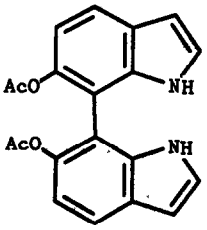

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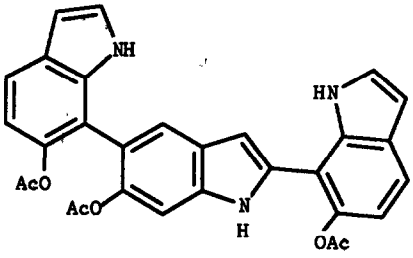

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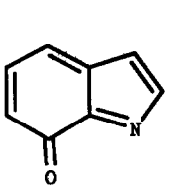
From consideration of the structure of compounds **9** -**19** it appears that the mode of polymerisation of hydroxyindoles **6**-**8** is governed to a significant extent by the position of the carbocyclic hydroxyl substituent. In the case of **6** , the relatively simple pattern of reactivity coupled with the prevailing presence of C3-C4 linkages in the oligomeric products would be in favour of an ionic type of polymerisation involving probably the initial formation of the quinonimine **20** . This would subsequently undergo attack at the 4- and 6-positions by the nucleophilic sites of a 7-hydroxyindole counterpart. Such a positional reactivity is consistent with the higher stability of the intermediate adducts **21** and **22** with respect to the other possible

C-5 adduct **23**, in which the aromatic character of the condensed pyrrole moiety would be disrupted[12].



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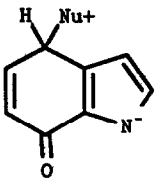

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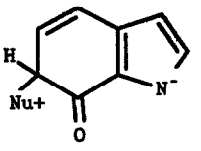

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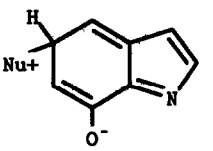

23

As far as the mechanism of oxidation of the other two hydroxyindoles **7** and **8** is concerned, the involvement of o- or p-quinonemethideimine type intermediates is less apparent. On the basis of the commonly accepted mechanism for the periodate oxidation of phenols[18,19], one could speculate that the oxidative polymerisation of these hydroxyindoles is initiated by two-electron transfer to the IO_4^-, leading to an electrophilic transient species, formally a phenoxonium cation, which is susceptible to nucleophilic attack by the starting hydroxyindole. In this connection it is worth noting that the nucleophilic reactivity of the hydroxyindole ring system is localised predominantly on the carbocyclic positions *ortho* or *para* to the hydroxyl substituent as well as on the enamine like 3-position. A notable exception is represented by the 6-hydroxy isomer **8** in which the electron releasing effect of the hydroxyl group elicits an unusual reactivity at the 2-position as evidenced by the predominant mode of polymerisation *via* C2-C7 linkages.

Experimental

M.ps. were determined with a Kofler hot-stage apparatus and are uncorrected. UV spectra were performed with a Perkin-Elmer Lambda 7 spectrophotometer. ^{1}H NMR (270 MHz) and ^{13}C NMR (67.9 MHz) spectra were recorded on a Bruker AC 270 spectrometer, in acetone-d_6 with TMS as internal standard. Electron impact mass spectra were determined with a Kratos MS-50 mass spectrometer. Besides molecular ions, the most abundant ions in the mass spectra (above m/z 100) are given with their relative intensities. Analytical and preparative TLC were carried out on precoated silica gel F-254 plates from Merck (0.25 and 0.50 mm layer thickness). Flash chromatography was performed on a silica column packed with Merck Kieselgel (230-400 mesh). 4-Hydroxyindole was from Aldrich Chemie (Steinheim, FRG). 6-Hydroxyindole and 7-hydroxyindole were prepared by debenzylation of 6- and 7-benzyloxyindole (Sigma Chemical Corp., St. Louis, Missouri, USA) with 5% Pd/C-ammonium formate in methanol[20].

For kinetic measurements, a 10^{-4} M solution of the hydroxyindole in 0.1 M phosphate buffer, pH 7.0 was oxidised with 2.2×10^{-4} M periodate. Reaction rates were determined by monitoring changes in optical density at the absorption maxima of the hydroxyindoles vs. time.

General procedure for the oxidation of hydroxyindoles 6-8

To a stirred solution of the hydroxyindole (2.5 mmol) in 0.1 M phosphate buffer, pH 7.0, a solution of sodium periodate (2.5 mmol) in water (50 ml) was added. After ten minutes, the reaction mixture was treated with sodium dithionite and repeatedly extracted with ethyl acetate. The combined organic layers were washed with water, dried over sodium sulphate and evaporated to dryness. The residue so obtained was acetylated with acetic anhydride and pyridine.

7-hydroxyindole (6)

The acetylated mixture was thin layer chromatographed on silica with $CHCl_3$-MeOH (92:8) to give three main bands. The less polar band was further purified by preparative TLC ($CHCl_3$-MeOH 97:3) affording **9** (37 mg, Rf 0.53 in $CHCl_3$-MeOH 92:8) and **11** (31 mg, Rf 0.50 in $CHCl_3$-MeOH 92:8). The second band consisted of pure **12** (35 mg, Rf 0.41 in $CHCl_3$-MeOH 92:8), whereas the third more polar band was subjected to further purification on silica gel plates using $CHCl_3$-MeOH (95:5) as the eluent to give **13** (50 mg, Rf 0.33 in $CHCl_3$-MeOH 92:8).

7,7'-diacetoxy-4,4'-biindolyl (9).

Colourless prisms from benzene-AcOEt, m.p. 252-253 °C ; λ_{max} (EtOH) 305 nm (log ε 4.04); HRMS m/z 348.1071 (M^+) (calc. for $C_{20}H_{16}N_2O_4$ 348.1110); EIMS m/z 348 (M^+, 45), 306 (27), 264 (100); ^1H NMR δ(ppm): 2.34 (3Hx2,s,-CH_3), 6.52 (1Hx2,dd, J=3.1, 2.1 Hz, H-3, H-3'), 7.03 (1Hx2, d, J=7.8 Hz, H-6, H-6'), 7.24 (1Hx2,d, J=7.8 Hz, H-5, H-5'), 7.32 (1Hx2,dd, J=2.9, 2.9 Hz, H-2, H-2'), 10.62 (1Hx2, bs, NH, N'H); ^{13}C NMR δ(ppm): 20.96 (q, -CH_3), 103.36 (d, C-3, C-3'), 114.68 (d, C-6, C-6'), 120.66 (d, C-5, C-5'), 125.89 (d, C-2, C-2'), 129.44 (s, C-4, C-4'), 130.27 (s, C-9, C-9'), 131.77 (s, C-8, C-8'), 136.81 (s, C-7, C-7'), 169.52 (s, -CO-).

7,7'-diacetoxy-3,4'-biindolyl (10).

Colourless needles from benzene-AcOEt, m.p. 217-218 °C; λ_{max} (EtOH) 300 nm (log ε 4.17); HRMS m/z 348.1079 (M^+) (calc. for $C_{20}H_{16}N_2O_4$ 348.1110; EIMS m/z 348 (M^+, 59), 306 (44), 264 (100); ^1H NMR δ (ppm): 2.35 (3H,s, -CH_3), 2.36 (3H, s, -CH_3), 6.65 (1H, dd, J=2.8, 2.1 Hz, H-3'), 6.98 (1H, dd, J= 7.8, 1.0 Hz, H-6), 7.00 (1H, d, J=7.8 Hz, H-6'), 7.09 (1H, dd, J=7.8, 7.8 Hz, H-5), 7.27 (1H, d, J=7.8 Hz, H-5'), 7.33 (1H, dd, J=2.8, 2.8 Hz, H-2'), 7.61 (1H, d, J=2.5 Hz, H-2), 7.68 (1H, dd, J=7.8, 1.0 Hz, H-4), 10.52 (1H, bs, NH), 10.75 (1H, bs, N'H); ^{13}C NMR δ(ppm): 20.79 (3H,s, -CH_3), 20.94 (3H, s, -CH_3), 103.29 (d, C-3'), 114.84, 114.94 (d, d, C-6, C-6'), 117.61 (s, C-3'), 118.40 (d, C-4), 119.72 (d, C-5'), 120.12 (d, C-5), 124.64 (d, C-2), 125.70 (d, C-2'), 125.90, 126.24 (s,s, C-9, C-9'), 129.99 (s, C-8), 130.06 (s, C-4'), 130.34 (s, C-8'), 136.22, 137.74 (s,s, C-7, C-7'), 169.46, 169.56 (s,s, -CO-).

7,7',7"-triacetoxy-3,4':6',4"-terindolyl (11).

Colourless oil; λ_{max} (EtOH) 296 nm; HRMS m/z 521.1601 (M^+) (calc. for $C_{30}H_{23}N_3O_6$: 521.1586); EIMS m/z 521 (M^+, 53), 479 (100), 437 (35), 395 (36); ^1H NMR δ(ppm): 2.34 (3H, s, -CH_3), 2.35 (3Hx2, s, -CH_3), 6.53 (1H, dd, J=3.1, 2.0 Hz, H-3'), 6.71 (1H, dd, J=3.1, 2.0 Hz, H-3"), 6.96 (1H, dd, J= 7.9, 0.8 Hz, H-6), 7.00 (1H, d, J= 7.9 Hz, H-6"), 7.07 (1H, dd, J= 7.9, 7.9 Hz, H-5), 7.12 (1H, d, J=7.9 Hz, H-5"), 7.33 (1H, dd, J= 3.1, 3.1 Hz, H-2'), 7.38 (1H, dd, J=3.1, 3.1 Hz, H-2"), 7.50 (1H, s, H-5'), 7.70 (1H, d, J= 2.5 Hz, H-2), 7.74 (1H, dd, J= 7.9, 0.8 Hz, H-4), 10.51, 10.58, 10.69 (1H each, bs, NH, N'H, N"H); ^{13}C NMR δ(ppm): 20.74 (q, -CH_3), 20.88 (q, -CH_3), 103.23, 103.27 (d,d, C-3', C-3"), 114.39, 114.89 (d,d, C-6, C-6"), 117.45 (s, C-3), 118.36 (d, C-4),120.14 , 121.04 (d,d, C-5', C-5"), 122.63 (d, C-5), 124.82 (d, C-2), 125.97, 126.02 (d,d,

C-2′, C-2"), 127.03 (s, C-6′), 129.05, 129.25, 129.62 (s,s,s, C-9, C-9′, C-9"), 129.95, 130.31 (s,s, C-4′, C-4"), 130.85, 130.87, 130.88 (s,s,s, C-8, C-8′, C-8"), 133.35 (s, C-7′), 136.75 (s, C-7"), 137.69 (s, C-7), 169.41 (s, -CO-).

7,7′,7",7‴-tetraacetoxy-3,4′:6′,6":4",3‴-tetraindolyl (12). Colourless prisms from THF, m.p. 207-209 °C; λ_{max} (EtOH) 292 nm (log ε 4.54); HRMS m/z 694.2112 (M^+) (calc. for $C_{40}H_{30}N_4O_8$ 694.2064); EIMS m/z 694 (M^+, 60), 652 (75), 610 (100), 568 (72), 525 (46); ^{1}H NMR δ(ppm): 2.14 (3Hx2, $-CH_3$), 2.35 (3Hx2, $-CH_3$), 6.73 (1Hx2, dd,J=3.1, 1.9 Hz, H-3′, H-3"), 6.98 (1Hx2, dd, J= 7.6, 0.8 Hz, H-6, H-6‴), 7.11 (1Hx2, dd, J=7.6, 7.6 Hz, H-5, H-5‴), 7.37 (1Hx2, dd, J=3.1, 3.1 Hz, H-2′, H-2"), 7.44 (1Hx2,s, H-5′, H-5"), 7.68 (1Hx2, d, J=2.5 Hz, H-2, H-2‴), 7.80 (1Hx2, dd, J= 7.6, 0.8 Hz, H-4, H-4‴), 10.52 (1Hx2,bs, NH, N‴H), 10.63 (1Hx2, bs, N′H, N"H); ^{13}C NMR δ(ppm): 20.81 (q, $-CH_3$), 20.96 (q, $-CH_3$), 103.28 (d, C-3′, C-3"), 114.99 (d, C-6, C-6‴), 117.44 (s, C-3, C-3‴), 118.45 (d, C-4,C-4‴), 120.24 (d, C-5′,C-5"), 123.04 (d, C-5,C-5‴), 124.87 (d, C-2, C-2‴), 125.00, 125.98 (s,s, C-9, C-9′, C-9", C-9‴), 126.10 (d, C-2′, C-2"), 129.29 (s, C-6′, C-6"), 130.05 (s, C-4′, C-4"), 130.37, 130.62 (s,s, C-8, C-8′, C-8", C-8‴), 133.87 (s, C-7′, C-7"), 137.76 (s, C-7, C-7‴), 169.50 (s, -CO-), 169.52 (s, -CO-).

4-Hydroxyindole (7)

Flash chromatography of the acetylated mixture on a 2.5 x 35 cm column using $CHCl_3$ containing from 1% to 4% methanol as the eluent, gave three main fractions. Two of these were further purified on silica gel plates with $CHCl_3$-MeOH 98:2 and 97:3 to give **13** (23 mg, Rf 0.89 in $CHCl_3$-MeOH 96:4) and **14** (16 mg, Rf 0.49 in $CHCl_3$-MeOH 96:4), respectively, whereas compounds **16** (6 mg, Rf 0.47 in $CHCl_3$-MeOH) and **15** (30 mg, Rf 0.35 in $CHCl_3$-MeOH 96:4) were obtained by TLC purification ($CHCl_3$-MeOH 96:4) of the third more polar fraction.

4,4′-diacetoxy-7,7′-biindolyl (13). Colourless oil; λ_{max}(EtOH) 286 nm; HRMS m/z 348.1130 (M^+) (calc. for $C_{20}H_{16}N_2O_4$ 348.1110); EIMS m/z 348 (M^+, 27), 306 (19), 264 (100); ^{1}H NMR δ: 2.39 (3Hx2,s, $-CH_3$), 6.49 (1Hx2,dd, J=2.8, 1.9 Hz, H-3,H-3′), 6.89 (1Hx2,d, J=7.8 Hz,H-5,H-5′), 7.22 (1Hx2,d, J=7.8 Hz, H-6, H-6′), 7.30 (1Hx2, dd, J=2.8, 2.8 Hz, H-2, H-2′), 10.22 (1Hx2, bs, NH, NH′); ^{13}C NMR δ: 20.91 (q, $-CH_3$), 99.69 (d, C-3,C-3′), 112.63 (d, C-5,C-5′), 121.05 (s, C-7,C-7′), 122.86 (d,C-6,C-6′), 122.99(s, C-9, C-9′), 126.38(d, C-2,C-2′), 136.79 (s, C-8,C-8′), 144.41 (s, C-4, C-4′), 169.50 (s, -CO-).

4,4′,4"-triacetoxy-5,5′:7′,7"-terindolyl (14). Colourless oil; λ_{max} 285 nm; HRMS m/z 521.1598 (M^+) (calc for $C_{30}H_{23}N_3O_6$ 521.1586); EIMS m/z 521 (M^+, 23), 479 (54), 437 (58), 395 (100); ^{1}H NMR δ: 2.10 (3H,s,$-CH_3$), 2.11 (3H,s,$-CH_3$), 2.37 (3H,s,$-CH_3$), 6.39 (1H,ddd, J=2.8, 2.2, 0.8 Hz, H-3), 6.46 (1H, dd, J=2.6, 2.2 Hz, H-3"), 6.47 (1H, dd, J=2.6, 2.2 Hz, H-3′), 6.89 (1H,d, J=7.8 Hz, H-5"), 7.15 (1H,d, J=8.3 Hz, H-6), 7.22 (1H,s, H-6′), 7.28 (1H,d, J=7.8, H-6"), 7.29 (1H, dd, J= 2.8, 2.8 Hz, H-2), 7.32 (1H, dd, J= 2.6, 2.6 Hz, H-2"), 7.33 (1H, dd, J=2.6, 2.6 Hz, H-2′), 7.36 (1H, dd, J=8.3,0.8 Hz, H-7), 10.38 (2H, bs, N′H, N"H), 10.51 (1H, bs, NH); ^{13}C NMR δ: 20.83 (q, $-CH_3$), 20.84 (q, $-CH_3$), 99.74, 100.09, 100.48 (d,d,d, C-3, C-3′, C-3"), 109.80 (d, H-7), 112.67 (d, C-5"), 120.89, 121.06 (s,s,C-7′, C-7"), 122.19 (s, C-5), 122.95 (d, C-6), 123.02 (d, C-6′), 123.10 (d, C-6"), 123.64 (s, C-5′), 125.61, 126.08 (s,s, C-9, C-9"), 126.35 (d, C-2"), 126.36 (d, C-2′), 126.47 (d,C-2), 126.68 (s, C-9′), 136.01, 137.37, 138.65 (s,s,s, C-8, C-8′, C-8"), 144.54 (s, C-4′), 144.56 (s, C-4), 147.52 (s, C-4"), 169.68 (s, -CO-), 169.70 (s, -CO-), 169.75 (s, -CO-).

4,4',4"-triacetoxy-3,7';5',5"-terindolyl (15).
Colourless prisms from benzene -AcOEt, m.p. 172-174 ; λ_{max} (EtOH) 277 nm (logϵ 4.16);HRMS m/z 521.1549 (M^+) (calc. for $C_{30}H_{23}N_3O_6$ 521.1586); EIMS m/z 521 (M^+, 38), 479 (77), 437 (85), 395 (100); ^{1}H NMR δ(ppm): 1.33 (3H,s, $-CH_3$), 2.09 (3H,s,$-CH_3$), 2.15 (3H,s, $-CH_3$), 6.36 (1H, ddd, J=2.7, 1.9, 0.8 Hz, H-3"), 6.44 (1H,dd, J=3.0, 2.0 Hz,H-3'), 6.68 (1H,dd, J=7.6, 0.7 Hz, H-5), 7.04 (1H,s, H-6'), 7.12 (1H,dd, J=7.6, 7.6 Hz, H-6), 7.15 (1H,d, J=8.3 Hz, H-6"), 7.29 (1H, dd, J=2.7, 2.7 Hz, H-2"), 7.30 (1H, dd, J=2.7, 2.7 Hz, H-2") 7.32 (1H,dd, J=3.0, 3.0 Hz, H-2'), 7.34 (1H,dd, J=7.6, 0.7 Hz, H-7), 7.36 (1H,d, J=8.3 Hz, H-7"), 7.39 (1H,d, J=2.5 Hz, H-2),10.01 (1H,bs, N'H), 10.35 (1H,bs, NH), 10.57 (1H,bs, N"H); ^{13}C NMR δ(ppm): 19.57 (q,$-CH_3$), 20.70 (q,$-CH_3$), 20.88 (q,$-CH_3$), 99.92 , 100.35(d,d,C-3',C-3"), 109.76, 110.27 (d,d, C-7,C-7"), 112.36 (s, C-3), 113.25 (d, C-5), 118.06 (s, C-7'), 121.00, 122.22 (s,s, C-5', C-5"), 122.93 (d,C-6'), 122.56, 122,57 (d,d, C-6, C-6"), 123.05 (s, C-9), 125.37, 125.67 (d,d, C-2', C-2"), 125.82, 126.08 (s,s, C-9',C-9"), 127.60 (s, C-2), 137.91, 138.16, 139.55 (s,s,s, C-8, C-8', C-8"), 141.21, 142.15 (s,s, C-4',C-4"), 145.17 (s, C-4), 169.23, 169.38 (s,s, -CO-).

4,4',4",4'''-tetracetoxy-3,7';5',5";7",7'''-tetraindolyl (16).
Colourless oil; λ_{max} 284 nm; HRMS m/z 694.2105 (M^+) (calc. for $C_{40}H_{30}N_4O_8$ 694.2064); EIMS m/z 694 (M^+, 77), 652 (100), 610 (84), 568 (78), 525 (42); ^{1}H NMR δ (ppm): 1.31 (3H,s, $-CH_3$), 2.15 (3H, s, $-CH_3$), 2.21 (3H,s, $-CH_3$), 2.38 (3H,s,$-CH_3$), 6.45 (1Hx2,dd, J=2.9, 2.0 Hz, H-3", H-3''') 6.46 (1H, dd, J=3.0, 2.1 Hz, H-3'), 6.68 (1H, dd, J=7.6, 0.7 Hz, H-5), 6.91 (1H,d, J=7.8 Hz, H-5'''), 7.13 (1H,dd, J=7.6, 7.6, H-6), 7.14 (1H,s, H-6'), 7.27 (1H, d, J=7.8 Hz, H-6'''), 7.29 (1H, dd, J= 3.0, 3.0, H-2'), 7.31 (1H, dd,J= 2.9, 2.9, H-2"), 7.32 (1H,dd, J= 2.9, 2.9 Hz, H-2'''), 7.34 (1H,s, H-6"), 7.39 (1H,dd, J=7.6, 0.7, H-7), 7.45 (1H, d, J=2.7, H-2), 10.02 (1H, bs, N'H), 10.37 (2H, bs, N"H, N'''H), 10.68 (1H, bs, NH); ^{13}C NMR δ(ppm): 19.62 (q, $-CH_3$), 20.96 (q, $-CH_3$), 99.83, 100.01 (d,d,C-5,C-5'''), 100.83 (d, C-3'), 110.31 (d, C-7), 112.00 (s, C-3), 112.77, 113.37 (d,d, C-3,C-3'''), 119.65 (s, C-7'), 120.96, 121.15 (s,s, C-7",C-7'''), 122.00, 122.89 (s,s, C-5', C-5"), 122.65, 122.67 (d,d, C-6, C-6'), 123.03, 123.10, (d,d, C-6",C-6'''), 123.69, 125.53, 126.23, 126.25 (s,s,s,s, C-9, C-9', C-9", C-9'''), 126.53, 126.54, 126.56 (d,d,d, C-2', C-2", C-2'''), 127.63 (d, C-2), 135.37, 136.96, 138.13, 139.87 (s,s,s,s, C-8, C-8', C-8", C-8'''), 141.02, 141.53 (s,s, C-4', C-4"), 143.75, 143.96 (s,s, C-4, C-4'''), 169.47 (s,-CO-), 169.48 (s,-CO-), 169.50 (s,-CO-).

6-hydroxyindole (8)
Oxidation of 8 was carried out using 1.37 mmol of periodate . After work-up as above, the acetylated mixture was fractionated by flash chromatography on a 35x2.5 cm column using benzene containing from 10 to 25% of ethyl acetate as the eluent. The first pooled fractions were chromatographed on silica gel plates (benzene-AcOEt, 95:5) to give 18 (15 mg, Rf 0.60 in benzene-AcOEt 90:10) . The second and the third pooled fractions were similarly purified by TLC (benzene-AcOEt 90:10) affording, besides the starting material as 6-acetoxyindole (50 mg), 17 (50 mg, Rf 0.38 in benzene-AcOEt 90:10). Thin layer chromatography on silica of the fourth fraction (chloroform-MeOH 99:1) yielded 19 (10 mg, Rf 0.18 in benzene-AcOEt 90:10).

6,6'-diacetoxy-7,7'-biindolyl (18).
Colourless oil; λ_{max}(EtOH) 282 nm; HRMS m/z 348.1086 (M^+)(calc. for $C_{20}H_{16}N_2O_4$ 348.1110);EIMS m/z 348 (M^+, 6), 306 (36), 264 (100); ^{1}H NMR δ (ppm): 1.86 (3Hx2,s,$-CH_3$), 6.51 (1Hx2,dd, J= 3.0, 2.0 Hz, H-3, H-3'),

6.92 (1Hx2, d, J=8.5 Hz, H-5, H-5'), 7.22 (1Hx2,dd, J=3.0, 3.0 Hz, H-2,H-2'), 7.60 (1Hx2,d, J=8.5 Hz, H-4,H-4'), 9.60 (1Hx2,bs, NH,N'H); ^{13}C NMR δ (ppm): 21.11 (q, $-CH_3$), 110.69 (d, C-3, C-3'), 114.93 (d, C-5, C-5'), 121.73 (s, C-7, C-7'), 122.91 (d, C-4, C-4'), 125.62 (d, C-2,C-2'), 125.90 (s, C-9,C-9'), 137.46 (s,C-8,C-8'), 145.26 (s, C-6,C-6'), 170.31 (s,-CO-).

6,6'-diacetoxy-2,7'-biindolyl (17).

Colourless oil, λ_{max} (EtOH) 312 nm; HRMS m/z 348.1143 (M^+) (calc. for $C_{20}H_{16}N_2O_4$ 348.1110); EIMS m/z 348 (M^+, 50), 306 (39), 264(100); ^{1}H NMR δ(ppm) : 2.13 (3H,s,$-CH_3$), 2.27 (3H, s, $-CH_3$), 6.56 (1H,dd, J=3.1,1.9 Hz, H-3'), 6.73 (1H, dd, J=2.1,1.0 Hz, H-3), 6.82 (1H,dd, J=8.5, 2.0 Hz, H-5), 6.90 (1H,d, J= 8.5 Hz, H-5'), 7.25 (1H, dd, J=2.0, 1.0 Hz, H-7), 7.37 (1H, dd, J=3.1, 3.1 Hz, H-2'), 7.57 (1H, d, J= 8.5 Hz, H-4'), 7.59 (1H, d, J= 8.5 Hz, H-4), 10.45 (2H, bs, NH,N'H); ^{13}C NMR δ (ppm): 20.88 (q, $-CH_3$), 21.03 (q, $-CH_3$), 102.93 (d, C-3), 103.26 (d,C-3'), 105.23 (d, C-7), 111.02 (s,C-7'), 114.93, 115.74 (d,d, C-5,C-5'), 121.08, 121.24 (d,d, C-4, C-4'), 126.92 (d, C-2'), 127.39, 127.51 (s,s, C-9, C-9'), 132.48 (s, C-2), 135.47 (s, C-8'), 137.71 (s, C-8), 144.30 8s, C-6'), 147.55 (s, C-6), 169.99 (s, -CO-), 170.17 (s, -CO-).

6,6',6"-triacetoxy-7,5':2',7"-terindolyl (19).

Colourless oil; λ_{max}(EtOH) 263,282 nm; HRMS m/z 521.1578 (M^+) (calc. for $C_{30}H_{23}N_3O_6$ 521.1586); EIMS m/z 521 (M^+, 21), 479 (54), 437 (62), 395 (100); ^{1}H NMR δ(ppm): 1.87 (3H,s, $-CH_3$), 2.00 (3H, s, $-CH_3$), 2.24 (3H,s, $-CH_3$), 6.57 (1H,dd, J=3.0, 2.0 Hz, H-3") 6.62 (1H,dd, J=3.0, 2.0 Hz, H-3), 6.86 (1H, dd, J= 2.1, 1.0 Hz, H-3'), 6.93 (1H, d, J= 8.5 Hz, H-5"), 6.98 (1H,d, J=8.5 Hz, H-5), 7.32 (1H,dd, J= 3.0,3.0 Hz, H-2"), 7.42 (1H,d, J= 1.0 Hz, H-7'), 7.45 (1H,dd, J=3.0, 3.0 Hz, H-2), 7.57 (1H,d, J=8.5 Hz, H-4"), 7.59 (1H,s, H-4'), 7.62 (1H,d, J=8.5 Hz, H-4), 10.01 (1H, bs, N'H), 10.72 (1H, bs, N"H), 10.74 (1H,bs, NH); ^{13}C NMR δ(ppm): 20.76 (q, $-CH_3$), 20.94 (q, $-CH_3$), 21.15 (q, $-CH_3$), 102.63, 103.12 (d,d, C-3, C-3"), 103.55 (d, C-3'), 106.55 (d, C-7'), 114.11, 114.57 (s,s, C-7,C-7"), 115.71, 115.97 (d,d, C-5, C-5"), 120.22 (d, C-4'), 121.43, 123.08 (d,d, C-4, C-4"),124.99 (s, C-5'), 125.00, 126.80 (d,d, C-2, C-2"), 127.15, 127.77, 127.78 (s,s,s, C-9, C-9', C-9"), 133.15 (s, C-2'), 135.32, 136.80, 137.65 (s,s,s, C-8, C-8', C-8"), 144.31, 144.67 (s,s, C-6, C-6"), 145.31 (s, C-6'), 169.92, 170.09, 170.16 (s,s,s, -CO-).

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